UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,248	02/27/2007	Suk-Wah Tam-Chang	028.0002-US00	3055

92049 7590 07/13/2010

J.A. Lindeman & Co. PLLC
3190 Fairview Park Drive
Suite 480
Falls Church, VA 22042

EXAMINER	
SISSON, BRADLEY L	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
07/13/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@jalindeman.com
rhonda.grant@jalindeman.com
jeff.lindeman@jalindeman.com

Office Action Summary	Application No.	Applicant(s)	
	10/578,248	TAM-CHANG ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-15 and 25-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 April 2010* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/16/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Claims 1-15 and 25-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 29 June 2009.

Drawings

2. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because:

a. The lettering is not of proper size, uniform density, and well-defined in Figure(s) 5 and 7-11. See 37 CFR 1.84 (l) and (p)(1) – (5). ("Numbers, letters, and reference characters must measure at least .32 cm (1/8 inch) in height.")

3. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

Replacement Drawing Sheets

Drawing changes must be made by presenting replacement sheets which incorporate the desired changes and which comply with 37 CFR 1.84. An explanation of the changes made must be

presented either in the drawing amendments section, or remarks, section of the amendment paper. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). A replacement sheet must include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of the amended drawing(s) must not be labeled as "amended." If the changes to the drawing figure(s) are not accepted by the examiner, applicant will be notified of any required corrective action in the next Office action. No further drawing submission will be required, unless applicant is notified.

Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and within the top margin.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDONMENT of the application.

If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 16-24 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

6. Claim 16 is the only independent claim under consideration. For convenience, claim 16 is reproduced below.

> 16. (Original) A nucleic acid complex comprising an oligonucleotide hybridized to a fluorophore-labeled reporter sequence, wherein the oligonucleotide comprises a hairpin-forming sequence capable of forming a stem-loop, and wherein formation of the stem-loop modifies fluorescence signals of the reporter sequence when the reporter sequence is hybridized to the oligonucleotide.

7. As set forth in *In re Alonso* 88 USPQ2d 1849 (Fed. Cir. 2008), at 1851:

> The written description requirement of 35 U.S.C. § 112, ¶ 1, is straightforward: "The specification shall contain a written description of the invention …." To satisfy this requirement, the specification must describe the invention in sufficient detail so "that one skilled in the art can clearly conclude that the inventor invented the claimed invention as of the filing date sought." *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997); *see also LizardTech, Inc. v. Earth Res. Mapping, Inc.*, 424 F.3d 1336, 1345 [76 USPQ2d 1724] (Fed. Cir. 2005); *Eiselstein v. Frank*, 52 F.3d 1035, 1039 [34 USPQ2d 1467] (Fed. Cir. 1995).

Alonso at 1852:

> A genus can be described by disclosing: (1) a representative number of species in that genus; or (2) its "relevant identifying characteristics," such as "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Enzo*, 323 F.3d at 964.

8. In applying the test as set forth in *Alonso*, it is noted that applicant is claiming a genus of nucleic acid complexes. At the very least, the complex must comprise two molecules- an oligonucleotide comprising a hairpin-forming sequence capable of forming a stem-loop, and a "fluorophore-labeled reporter sequence."

9. Applicant, at page 10 of the disclosure, states:

> As used herein, an oligonucleotide can be a polynucleotide and comprise at least 10, 20, 30, 40, 50, or more nucleotide residues.

Using the embodiment of an oligonucleotide of but 200 nucleotides, which is encompassed by the expression "or more", and substituting those positions with the 4 conventional nucleotides, one realizes that there are 4^{200}, or 3.2×10^{120} different oligonucleotides. In putting these numbers in perspective, it is noted that the earth is estimated to have existed for 10^{17} seconds (see Creighton, T.E. 1983. Proteins: Structure and Molecular Principles, W. H. Freeman and Company, NY. 93-94, page 94, paragraph 1). There are an estimated 10^{79} atoms in the universe (see page 231 of Creighton, Prog. Bophys. Molec. Biol. 33:231-233, 1975). The aspect of providing all possible oligonucleotides that are 200 nucleotides in length would fill the entire universe 41 times over.

10. A review of the disclosure finds where applicant has provided a Sequence Listing as well as a further description in Table 6.

SEQ ID NO.	Length	Description (Sequence Listing)	Description (specification)
1	20	Artificial Sequence	Reporter Oligonucleotide, 5'-TAMARA labeled (p. 20)
2	20	Artificial Sequence	Reporter Oligonucleotide (p. 20)
3	79	Artificial Sequence	Capture Oligonucleotide (p. 20)
4	79	Artificial Sequence	Capture Oligonucleotide (p. 20)
5	24	Artificial Sequence	Target Sequence (p. 20)
6	67	Artificial Sequence	
7	20	Artificial Sequence	Address Oligonucleotide with Disulfide (AO/SS) (p. 20)
8	21	Artificial Sequence	Reporter Oligonucleotide, 5'-TAMARA-linked (Table 6, p. 28)

9	70	Artificial Sequence	Capture Oligonucleotide (Table 6, p. 28)
10	67	Artificial Sequence	B7-67mer (Table 6, p. 28)
11	15	Artificial Sequence	T3 (Table 6, p. 28)
12	15	Artificial Sequence	SM (Table 6, p. 28)

11. As presented above, applicant clearly contemplates oligonucleotides that are 10, 20, 30, 40, 50 or more nucleotide in length. A review of the disclosure fails to find where applicant has described any oligonucleotide, useful or not, that is 10, 30, 40, 50 or more nucleotides in length.

12. While applicant has claimed the nucleic acid complex of comprising an oligonucleotide that comprises a hairpin-forming sequence, and that this oligonucleotide is to hybridize to a fluorophore-labeled reporter sequence, applicant has not provided an adequate description of the genus of oligonucleotides that are useful, alone or in complexed formation so that one of skill in the art would be able to identify those that are useful from those that are not useful.

13. For purposes of examination, the reporter sequence acid has been construed as encompassing not only single-stranded nucleic acids, but also double-stranded nucleic acids, be it dsDNA, dsRNA, or DNA-RNA duplexes, and that the "hybridization" that is taking place between the oligonucleotide and the reporter sequence can result in the formation of either duplex or triplex strands.

14. Applicant has not described how the various genera of such molecules are to be used in any method that has utility under 35 USC 101. Indeed, as presented above, the "artificial sequences" set forth in Table 6, as well as in the Sequence Listing, present no embodiment of useful RNA molecules, no embodiment of triplex formation, and no embodiment of a useful

DNA complex, much less an adequate description of those molecules that are useful such that one of skill in the art would be able to recognize/distinguish useful from non-useful molecules.

15. It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

16. Accordingly, a review of the disclosure fails to find where either prong f the written description test set forth in *Alonso* has been satisfied. Therefore, and in the absence of convincing evidence to the contrary, claims 16-24 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Response to argument

17. At page 6 of the response of 13 January 2010, hereinafter the response, applicant asserts that they are not claiming an infinite number of molecules, but rather, the number of complexes claimed "is only limited by the total number of targets that one wishes to identify and/or measure."

18. In applying applicant's argument, if the limiting factor were only one's desire, then seemingly if one wishes to identify and/or measure an infinite number of molecules, then the

claim would encompass such a broad genus. Accordingly, this argument has not been found persuasive towards the withdrawal of the rejection.

19. At each of pages 6, 7, and 8 of the response argument is presented as to what one of skill in the art would have recognized and been able to understand and perform. These argument have been considered and have not been found persuasive as they are each conclusory in nature and void of any factual underpinning. Attention is directed to MPEP 2145.

> Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See MPEP § 2129 and § 2144.03 for a discussion of admissions as prior art.
> The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). See MPEP § 716.01(c) for examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration.

20. At page 8 of the response applicant states:

> Indeed, once one of skill in the art determines the necessary sequences to be included in the claimed nucleic acid complex based upon the target sequence, commercial suppliers could have synthesized it using routine steps. For example, the specification used molecules provided by integrated DNA Technologies, Inc. or Synthetic Genetics, Inc. (see Specification as-filed at I[[0068]), and other suppliers provide these services. The specification also discloses that computer programs, such as OligoAnalyzer 3°0, can be used to help ensure that the sequence to be made does not form self-dimers, unwanted hairpins, and cross-hybridization. See Specification as- filed at ¶[[0068].

21. The above argument has been considered and has not been found persuasive. The rejection is not one of enablement, which the response is seemingly directed to, but rather, one of inadequacy of written description. Claims to a product, not to a method of making same, presupposes that applicant already has possession of the genus of molecules/complexes claimed.

Accordingly, it is applicant that needs to have already selected and produced the genus of nucleic acid complexes. Such full and complete description of the genera of complexes claimed is not supported by the original disclosure. Further, applicant has not shown how the two oligonucleotides, each 20 nucleotides in length, and not directed to any useful reporter sequence, somehow constitute an adequate written description of the broad genera of molecules/complexes claimed. Further, applicant's response fails to address how the application as filed satisfies either prong of the written description test as set forth in *Alonso*.

22. For the above reasons and in the absence of convincing evidence to the contrary, the rejection is maintained.

Conclusion

23. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

24. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

26. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

27. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634